

Appl. No. To be assigned  
Amd. Dated April 8, 2004

**AMENDMENTS TO THE SPECIFICATION**

Please replace the paragraph which begins on page 1, line 7 with the following:

This is a continuation of U.S. Patent Application Serial No. 10/279,496 filed October 24, 2002, which is a continuation of U.S. Patent Application Serial No. 09/132,963 filed August 12, 1998, which is a continuation of U.S. Patent Application Serial No. 08/881,696 filed June 24, 1997, now U.S. Pat. 6,267,858, which is a continuation-in-part of U.S. Patent Application Serial No. 08/671,987 filed June 28, 1996, now U.S. Pat. 5,942,443, and U.S. Patent Application Serial No. 08/761,575 filed December 06, 1996, now U.S. Pat. 6,046,056 each of which is hereby incorporated herein by reference in its entirety for all purposes. A PCT Application designating the United States of America, WO 98/00231 ~~Attorney Docket No. 017646-00042PC~~, substantially identical to the present application was co-filed in the United States Receiving Office on June 24, 1997. This application is also incorporated herein by reference.

Please replace the paragraph that begins on page 11, line 12 with the following:

Biological responses are often triggered and/or controlled by the binding of a receptor to its ligand. For example, interaction of growth factors, i.e., epidermal growth factor (EGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), etc., with their receptors stimulates a wide variety of biological responses including, e.g., cell proliferation and differentiation, activation of mediating enzymes, stimulation of messenger turnover, alterations in ion fluxes, activation of enzymes, changes in cell shape and the alteration in genetic expression levels. Accordingly, control of the interaction of the receptor and its ligand may offer control of the biological responses caused by that interaction.

Please replace the paragraph that begins on page 18, line 10 with the following:

More generally, labels are commonly detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful nucleic acid labels include <sup>32</sup>P, <sup>35</sup>S, fluorescent dyes, electron-dense reagents, enzymes (e.g., as commonly used in an ELISA), biotin, dioxigenin, or haptens and proteins for which antisera or monoclonal

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antibodies are available. A wide variety of labels suitable for labeling biological components are known and are reported extensively in both the scientific and patent literature, and are generally applicable to the present invention for the labeling of biological components. Suitable labels include radionucleotides, enzymes, substrates, cofactors, inhibitors, fluorescent moieties, chemiluminescent moieties, magnetic particles, and the like. Labeling agents optionally include *e.g.*, monoclonal antibodies, polyclonal antibodies, proteins, or other polymers such as affinity matrices, carbohydrates or lipids. Detection proceeds by any of a variety of known methods, including spectrophotometric or optical tracking of radioactive or fluorescent markers, or other methods which track a molecule based upon size, charge or affinity. A detectable moiety can be of any material having a detectable physical or chemical property. Such detectable labels have been well-developed in the field of gel electrophoresis, column chromatography, solid substrates, spectroscopic techniques, and the like, and in general, labels useful in such methods can be applied to the present invention. Thus, a label is any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical thermal, or chemical means. Useful labels in the present invention include fluorescent dyes (*e.g.*, fluorescein isothiocyanate, Texas red, rhodamine, and the like), radiolabels (*e.g.*,  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$  or  $^{33}\text{P}$ ), enzymes (*e.g.*, LacZ, chloramphenicol acetyltransferase (CAT), horse radish peroxidase, alkaline phosphatase and others, commonly used as detectable enzymes, either as marker products or as in an ELISA), nucleic acid intercalators (*e.g.*, ethidium bromide) and colorimetric labels such as colloidal gold or colored glass or plastic (*e.g.* polystyrene, polypropylene, latex, *etc.*) beads.

Please replace the paragraph which begins on page 24, line 13 with the following:

The introduction of large numbers of individual, discrete volumes of test compounds into the sample is carried out by a number of methods. For example, micropipettors are optionally used to introduce the test compounds into the device. In preferred aspects, an electropipettor is used which is fluidly connected to sample channel 112. An example of such an electropipettor is described in, *e.g.*, U.S. Patent No. 5,779,868, ~~Application Serial No. 08/671,986, filed June 28, 1996 (Attorney Docket No. 017646-000500)~~ the disclosure of which is hereby incorporated herein by reference in its entirety for all purposes. Generally, this electropipettor utilizes electroosmotic fluid direction as described herein, to alternately sample a

number of test compounds, or "subject materials," and spacer compounds. The pipettor then delivers individual, physically isolated sample or test compound volumes in subject material regions, in series, into the sample channel for subsequent manipulation within the device. Individual samples are typically separated by a spacer region of low ionic strength spacer fluid. These low ionic strength spacer regions have higher voltage drop over their length than do the higher ionic strength subject material or test compound regions, thereby driving the electrokinetic pumping. On either side of the test compound or subject material region, which is typically in higher ionic strength solution, are fluid regions referred to as first spacer regions (also referred to as "guard bands"), that contact the interface of the subject material regions. These first spacer regions typically comprise a high ionic strength solution to prevent migration of the sample elements into the lower ionic strength fluid regions, or second spacer region, which would result in electrophoretic bias. The use of such first and second spacer regions is described in greater detail in U.S. Patent No. 5,779,868 ~~Application Serial No. 08/671,986, filed June 28, 1996,~~ (~~Attorney Docket No. 017646-000500~~) which is incorporated herein by reference.

Please replace the paragraph which begins on page 27, line 4 with the following:

From sample channel **112**, test compounds is periodically or serially introduced into the main channel **110** and into the stream of first and second components as fluid regions containing the test compound, also referred to as the "subject material regions." Where these test compounds have an effect on the interaction of the first and second elements, it will produce a deviation in the signal detected at the detection window corresponding to the subject material region. As noted above, typically, the various different test compounds to be injected through channel **112** will be separated by a first and even second spacer fluid regions to allow differentiation of the effects, or lack of effects, from one test compound to another. In those embodiments where electroosmotic fluid direction systems are employed, the spacer fluid regions may also function to reduce any electrophoretic bias that can occur within the test sample. The use of these spacer regions to drive the electroosmotic flow of fluids, as well as in the general elimination of electrophoretic bias within the sample or test compound or subject material regions is substantially described in U.S. Patent No. 5,779,868 ~~Application Serial No.~~

~~08/671,986, filed June 28, 1996 (Attorney Docket No. 017646-000500)~~, previously incorporated herein by reference.

Please replace the paragraph which begins on page 30, line 11 with the following:  
Incorporating this electroosmotic fluid direction system into the device shown in Figure 1 involves incorporation of an electrode within each of the reservoirs **104, 106 and 108**, and at the terminus of sample channel **112** or at the terminus of any fluid channels connected thereto, whereby the electrode is in electrical contact with the fluid disposed in the respective reservoir or channel. Substrate materials are also selected to produce channels having a desired surface charge. In the case of glass substrates, the etched channels will possess a net negative charge resulting from the ionized hydroxyls naturally present at the surface. Alternatively, surface modifications are optionally employed to provide an appropriate surface charge, e.g., coatings, derivatization, e.g., silanation, or impregnation of the surface to provide appropriately charged groups on the surface. Examples of such treatments are described in, e.g., Provisional Patent Application Serial No. 60/015,498, filed April 16, 1996 (~~Abandoned~~Attorney Docket No. ~~017646-002600~~) which is hereby incorporated herein by reference in its entirety for all purposes.

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